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EXAMINER

LY, CHEYNE D

ART UNIT PAPER NUMBER

1631

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/558,232	MANYAK ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Cheyne D Ly	1631	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-56,58-105,107,108,110-129 and 132-138 is/are pending in the application.
- 4a) Of the above claim(s) 4-9,11-13,24-26,29-32,58,65,66,69 and 111-119 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 10, 14-16, 18-23, 27, 28, 33-56, 59-64, 67, 68, 70-94, 96-105, 108, 110, 120-129, and 132-138 is/are rejected.
- 7) ☒ Claim(s) 17,95 and 107 is/are objected to.
- 8) ☒ Claim(s) 1-56,58-105,107,108,110-129 and 132-138 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
     If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
     a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |                                                                                                |                                                                              |
|------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                               | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)           | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ .                                   |

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**Office Action Summary**

Part of Paper No. 1103

### **DETAILED ACTION**

1. Applicants' arguments filed September 10, 2003 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. The withdrawal of claims 44 and 45 as specified in the previous Office Action, mailed March 10, 2003, has been removed.
3. The withdrawal of claims 4-9, 11-13, 24-26, 29-32, 58, 65, 66, 69, and 111-119 has been acknowledged.
4. The cancellation of claims 57, 106, 109, 130, and 131 has been acknowledged.
5. Claims 1-3, 10, 14-23, 27, 28, 33-56, 59-64, 67, 68, 70-105, 107, 108, 110, 120-129, and 132-138 are examined on the merits.

### **Clarification of Restriction Requirement**

6. Applicants state that Applicants do not understand which of the species listed in the written Restriction Requirement claims 45 and 58 are generic to. It is re-iterated that claims 45 and 58 are generic to species listed in the species election requirement (pages 3-6) in the previous action mailed January 13, 2003.

### **OBJECTIONS**

7. The amendment filed September 10, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall

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introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

8. Figures 1C, 1D, 2A, 3A, 7A, 7B, 7C, 8A, and 8B.

9. Insertion of amendments to the following pages: 16, 17, 19, 20, 22, 23, 26, 29, and 33.

10. It is acknowledged that Applicants argue that the subject matter of the amendments do not introduce new matter to the instant application since said application as filed incorporates the subject matter by reference from the Provisional Application No. 60/130,9912. However, the said subject matter being submitted in the said amendment is essential material that is being used to describe the invention. Further, the essential matter being submitted defines the critical limitations of claims 67, 68, 76-78, 87, 89, 96, 102, 108, and 100, which support that the said amendments to the specification comprising essential material. "In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates "essential material" by reference, or (4) a foreign application" (MPEP 608.01(p)(I)).

11. Applicant is required to cancel the new matter in the reply to this Office Action.

12. Claims 17, 95, and 107 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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**Claim Rejections - 35 USC § 112, First Paragraph**

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 35, 46, 59, 67, 68, 76-78, 87, 89, 96, 102, 108, 100, 110, and 132 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

15. THIS IS A NEW MATTER REJECTION.

16. This rejection is maintained with respect to claims 67, 68, 76-78, 87, 89, 96, 102, 108, and 100, as recited in the previous office action mailed March 10, 2003.

17. Applicants argue to overcome said rejection by amending the said claims to recite limitations that have been disclosed in the Provisional Application (60/130,9912), which has been incorporated by reference. Applicants' argument has been fully considered and found to be unpersuasive due to the subject matter being submitted in the said amendment is essential material that is being used to describe the invention. (See the above Objection §, ¶ 7-11).

18. The instant rejection has been extended to claims 35, 46, 59, 110, and 132 due to the amended claims comprising NEW MATTER.

19. This rejection is necessitated by Applicants amendments.

20. Claims 35, lines 2 and 4; 46, line 3; 59, line 3; 132, line 2, recite the limitation of synthetic chemical compounds which has not been found in the instant specification.

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21. Claim 110, lines 3 and 4, recite the limitations of “non-steroidal”, “steroidal”, and “testosterone” which have not been found in the instant specification.

***Claim Rejections - 35 USC § 102***

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

23. Claims 1-3, 14-23, 27, 28, 33-45, 54-56, 59-64, 70-76, 78, 80, 89-91, 93, 94, 97-101, 102-106, 120, 121, 124, 125, and 127-132 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Goto et al. (1998).

24. This rejection is maintained with respect to claims 1-3, 14-23, 27, 28, 33-43, 54-56, 59-64, 71-75, 78, 80, 89-91, 93, 94, 97-101, 103-106, 120, 121, 125, and 127-132, as recited in the previous office action mailed March 10, 2003.

25. The instant rejection has been extended to claims 44, 45, 70, 76, 102, and 124.

26. This rejection is necessitated by Applicants amendments.

**RESPONSE TO APPLICANT’S ARGUMENT**

27. Applicant argues that Goto et al. does not disclose at least a third database containing records corresponding to tests of interactions between compounds in the first database and molecular targets in the second databases. Applicant’s argument has been fully considered and found to be unpersuasive as discussed below. “A schematic diagram showing LIGAND as an interface of KEGG (Kyoto Encyclopedia of Genes and Genomes) and DBGET/LinkDB systems as well as an interface of biological and chemical databases” (Figure 3, page 596).

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As cited above, Ligand is a component of a large system which includes more than the Ligand chemical database as pointed to by Applicant in arguing that Goto et al. only discloses a system consisting of two sections: ENZYME and COMPOUND. LIGAND is tightly coupled with the KEGG metabolic pathway database (page 592, column 1, line 52 to column 2, lines 4). Entry EC 2.2.1.1 from the ENZYME section (third database) is directed to tests of interactions as supported by the Comment section (a thiamine-diphosphate protein, wide specificity for both reactant...show high activity with D-erythrose as acceptor (effect)). The cofactor thiamine-diphosphate is from the COMPOUND section (second database) and GENES is from KEGG (first database) (Figures 1 and 3).

28. Specific to claims 33, 37, and 54, Applicant argues that the amended claims have overcome the instant rejection. Applicant argument via amendment has been fully considered and found to be unpersuasive due to the amended claims comprising NEW MATTER.

29. It is re-iterated Goto et al. (1998) discloses KEGG as a computerized database of mechanisms of gene functions and cellular functions in terms of the information pathways that consist of interacting genes or molecules (Page 591, Column 1, Lines 23-26).

30. Goto et al. teaches “new activities of computational functional genomics that include the identification of biological functions of unknown gene products,...comparative analysis of genes and genomes in different species, and analysis and simulation of gene expressions in different cells or in different developmental stages. In order to facilitate such post-genomic sequencing analyses, it has become a high priority to construct a new breed of database that



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defines functional aspects of genes, cells and organisms” (Page 591, Column 2, Lines 12-22).

The disclosure by Goto et al. above anticipates the limitations of claims 78 and 128-131.

31. The sequence data is capture from recent progress in genome sequencing from bacteria to eukaryotes (screening process) as directed to biological function (page 591, column 2, lines 9-22), as in instant claims 70 and 76.

32. “A schematic diagram showing LIGAND as an interface of KEGG (Kyoto Encyclopedia of Genes and Genomes) and DBGET/LinkDB systems as well as an interface of biological and chemical databases” (Figure 3, page 596). LIGAND comprises data directed to PIR superfamily (page 597, column 1, lines 11-14), as in instant claim 124.

33. “As illustrated in Figure 3, Ligand is a major component of the KEGG and DBGET/LinkDB systems. It makes connections between the factual data for individual molecules, i.e. genes and gene products, and the biological relationships among them, i.e. molecular interactions and molecular pathways” (Page 595, Column 2, Lines 1-2 and Page 596, Column 1, Lines 1-4). The KEGG project includes databases such as PATHWAY, COMPOUND, GENES and interaction databases such as ENZYME for enzymatic reactions and BRITE for molecular interactions in general. Specific to the BRITE database, molecular interactions may include those determined from the yeast two-hybrid system for protein-protein interaction (Page 597, Lines 32-46). The disclosure by Goto et al. above anticipates the limitations of claims 1, 3, 27, 33, 41, 63, 64, 103, 104, 125, 127 and 132.

34. The ENZYME database includes such enzymes as transferases, for example (Page 592, Column 2, Lines 15-16). “The DBGET/LinkDB system is especially suited to search information on related entries in other databases” (Page 594, Column 1, Lines 8-9).

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“LIGAND now consists of two sections: the expanded ENZYME section and the new COMPOUND section...The COMPOUND section is a collection of metabolic compounds, including substrates, products, inhibitors, cofactors and effectors, and other chemical compounds that play important functional roles in living cells” (Page 592, Column 1, Lines 49-53), as in claim 2 of this instant application.

35. “Each compound is given an accession number in the ENTRY field, which is followed by the compound name and its synonyms in the NAME field, and the molecular formula in the FORMULA field” (Page 593, Column 2, Lines 10-13). Tables 1 and 2 disclose the number of links from ENZYME to other databases where users can view information for enzymes whose roles in the metabolic pathways are known and whose sequences and three-dimensional structures have been determined (Page 594, Column 2, Lines 13-17), as in claims 97-99 and 120 of this instant application. The number of entries such as inhibitors or effectors and links in COMPOUND are disclosed in Table 4 (Page 595). The disclosure by Goto et al. above anticipates the limitations of claims 14-23, 28, 34-40, 42, 43, 54-56, 59-62, 67, 68 and 106.

36. “The LIGAND database thus provides fundamental data on both biological and chemical aspects of life” (Page 592, Column 2, Lines 4-5). “The DISEASE field describes human genetic disorders caused by a lack of or mutation of the enzyme, which is linked to the OMIM database. The MOTIF field describes the protein sequence motifs that are linked to PROSITE...and the STRUCTURE field contains the code names of the protein three-dimensional structures in the Protein Data Bank” (Page 593, Column 1, Lines 11-19). “The chemical structure is entered in our database in the MDL MOL file format, which can also be

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downloaded in DBGET/LinkDB to launch a helper application, such as ISIS/Draw, to view and manipulate the structure, as in claims 93 and 94 of this instant application. Because this file contains the information on atoms and bond of each compound, it may be used to reconstruct a three-dimensional structure of the compound. The last portion of the COMPOUND entry contains link information to other databases...The DBLINKS field includes the CAS (Chemical Abstract Services) registry number. The COMPOUND section is constructed manually, except for the link information to ENZYME and KEGG/PATHWAY, by consulting with various sources, such as the Merck Index (Budavari, 1996), and dictionaries of biochemistry and organic chemistry” (Page 593, Column 2, lines 28-32).

37. The inclusion of a document containing the description of the Merck Index is provided to support and expand on prior art cited from Goto et al. The Merck Index has the following type of information available: biological products, environmentally significant compounds, and natural products. “The MERCK INDEX ONLINE is made available through major online database vendors” (Page V, Lines 13-15 and 31-32). Specifically, the drug information disclosed in the Merck Index include the following: compound name, compound type, references to pharmacological or biological activity, clinical trials, toxicity studies, structure, and physical data which includes solubilities determined at room temperature, therapeutic category, metabolism in humans (Page ix and Page x, Lines 17-19, Structure section, Physical Data section, and Literature References section). The disclosure by Goto et al. above anticipates the limitations of claims 53, 89-91, 100-102.

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38. "LIGAND database provides the enzyme classification according to EC number...For instance, the sequence similarity can be used to define a hierarchical classification of families and superfamilies of functionally related proteins...The sequence and structural motifs that have been extracted from groups of enzymes with similar functions can also be considered as a functional hierarchy" (Page 596, Lines 24-26 and 30-33), as in claims 105 and 121 of this instant application.

39. Further, LinkDB provide access to ATPase EC 3.6.1.3, which is further linked to literature source via the ENZYME nomenclature database (ExPASy) that provide disclosure for ATPase in regard to binding and inhibition assays. A document by Liu et al. (1997) is provided not as prior art but only as disclosure to the data that is accessible via LinkDB. From LinkDB, EC 3.6.1.3 provides a link to reference literature via ExPASy specific to ATPase. For example, Liu et al. discloses "the assay uses  $Mg^{2+}$  ions to permeabilize membrane vesicles or proteoliposomes, thus allowing access of ATP to both sides of the bilayer. HisQMP2 displays a low level of intrinsic ATPase activity in the absence of HisJ; unliganded HisJ stimulates the activity and liganded HisJ stimulates to an even higher level. All three levels of activity display positive cooperativity for ATP with a Hill coefficient of 2 and a  $K_{0.5}$  value of 0.6 mM. The activity has been characterized with respect to pH, salt, phospholipids, substrate, and inhibitor specificity. Free histidine has no effect" (Abstract). "Vanadate, a potent inhibitor of P-type ATPases and histidine transport, inhibits the activity of HisQMP2, giving 50% inhibition at 6.5  $\mu M$ . Bafilomycin A1 (100  $\mu M$ ), ouabain (up to 3 mM), and  $NaN_3$  (10 mM) do not inhibit" (Page 21887, column 2, lines 23-28). The disclosure by Goto et al. above anticipates the limitations of claims 71-75 and 80.

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40. Claims 1, 10, 46-53, 57, 59, 67, 68, 79, 81-86, 92, 108, 109, 122-123 and 133-138 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Ogata et al. (1999).

41. This rejection is maintained with respect to claims 1, 10, 46-53, 57, 59, 67, 68, 79, 81-86, 92, 108, 109, 122-123 and 133-138, as recited in the previous office action mailed March 10, 2003.

#### **RESPONSE TO APPLICANT'S ARGUMENT**

42. Applicant argues that for the same reason as Goto et al., Ogata et al. does not disclose at least a third database containing records corresponding to tests of interactions between compounds in the first database and molecular targets in the second databases. Applicant argument has been fully considered and found to be unpersuasive as discussed below. It is re-iterated KEGG is tightly integrated with the LIGAND chemical database for enzyme reactions as well as with most of the major molecular biology databases by the DBGET/LinkDB system" (Page 29, Column 2, Lines 1-6). "First, KEGG aims at computerizing the current knowledge of genetics, biochemistry, and molecular and cellular biology in terms of the pathway of interacting molecules or genes...Second, KEGG maintains the gene catalogs for all organisms with completely sequenced genomes and selected organisms with partial genomes..." Third, KEGG maintains the catalog of chemical elements, compounds, and other substances in living cells as the LIGAND database" (Page 29, Column 2, Lines 23-29, 33-36, 42-43; Page 30, Column 1, Line 1).

43. The inclusion of citations from Goto et al. is not being used as prior art, but only to expand on the capabilities of LIGAND which is disclosed by Ogata et al. "A schematic

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diagram showing LIGAND as an interface of KEGG (Kyoto Encyclopedia of Genes and Genomes) and DBGET/LinkDB systems as well as an interface of biological and chemical databases” (Goto et al., Figure 3, page 596). Ligand is a component of a large system which includes more than the Ligand chemical database as pointed to by Applicant in arguing that Goto et al. only discloses a system consisting of two sections: ENZYME and COMPOUND. LIGAND is tightly coupled with the KEGG metabolic pathway database (Goto et al., page 592, column 1, line 52 to column 2, lines 4). Entry EC 2.2.1.1 from the ENZYME section (third database) is directed to tests of interactions as supported by the Comment section (a thiamine-diphosphate protein, wide specificity for both reactant...show high activity with D-erythrose as acceptor (effect)). The cofactor thiamine-diphosphate is from the COMPOUND section (second database) and GENES is from KEGG (first database) (Goto et al., Figures 1 and 3).

44. Specific to claim 46, Applicant argue that the amended claims have overcome the instant rejection. Applicant argument via amendment has been fully considered and found to be unpersuasive due to the amended claims comprising NEW MATTER.

45. Specific to claims 79 and 81-86, Applicant argues that it is not necessarily true that in ligand-receptor binding assays, the yeast two-hybrid system, or microarray expression assay interactions are determined by some potency value or compared to some specified threshold value. It is merely a possibility. Applicant’s argument has been fully considered and found to be unpersuasive as discussed below. It is well-known in the art that microarray expression assay interactions are determined by some potency value or compared to some specified threshold value. Specifically, microarray expression assays are widely used for their

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capability to detect fold changes in the expression of a plurality of genes. It is not “merely a possibility” that the results from microarray expression assays are determined by some potency value or compared to some specified threshold value, but the inherent feature of said assays that allows one detect change of expression of a plurality of genes.

46. It is re-iterated Ogata et al. discloses KEGG is tightly integrated with the LIGAND chemical database for enzyme reactions as well as with most of the major molecular biology databases by the DBGET/LinkDB system” (Page 29, Column 2, Lines 1-6). “First, KEGG aims at computerizing the current knowledge of genetics, biochemistry, and molecular and cellular biology in terms of the pathway of interacting molecules or genes...Second, KEGG maintains the gene catalogs for all organisms with completely sequenced genomes and selected organisms with partial genomes...” Third, KEGG maintains the catalog of chemical elements, compounds, and other substances in living cells as the LIGAND database” (Page 29, Column 2, Lines 23-29, 33-36, 42-43; Page 30, Column 1, Line 1), as in claims 47-49, 52 and 53 of this instant application.

47. “The user may enter the KEGG system top-down starting from the pathway information or bottom-up starting from the genomic information” (Page 30, Column 1, Lines 16-18) as in claim 50 and 51 of this instant application. “The co-linearity of genes between two genomes is quite useful for identification of clusters of orthologous genes. KEGG provides the comparative genome map for identification of such clusters and for functional annotation of newly sequenced genomes (Page 33, Column 1, Lines 33 and Figure 3). Table 3 shows the list of currently available tools such as gene cluster search and sequence similarity search for

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search and analysis of KEGG pathway maps and genome maps (Page 33, Column 2, Lines 54-55), as in claims 122-123 of this instant application.

48. The KEGG biochemical pathways include Ligand-Receptor Interaction (Page 30, Table 2, Cell Processes) as in claims 10, 67, 68, 108 and 109 in this instant application.

49. Ogata et al. further discloses “a typical ABC transporter consists of a substrate-binding protein, two membrane proteins, and two-ATP-binding proteins. “For example the KEGG reference pathways can be used to uncover molecular interactions and pathways that underlie gene expression profiles obtained by microarray experiments” (Page 30, Column 1, Lines 9-11). “A binary relation can be a substrate-product relation in metabolic pathways, a gene-gene interaction observed in gene expression profiles, or a protein-protein interaction observed by yeast two-hybrid system experiments” (Page 34, Column 1, Lines 34-37), as in claims 134-138 of this instant application.

50. “Thus, it is easy to see how the information of gene expression profiles can be used as still another constraint against the KEGG reference pathway maps. In fact, KEGG provides a tool to color the pathway maps in order to visualize, for example, the microarray patterns of gene expression profiles” (Page 33, Column 2, Lines 48-53). It is inherent in such techniques as the ligand-receptor binding assays, yeast two-hybrid system and microarray expression assays that interactions are determined by some potency value or compared to some specified threshold value, as in claims 79 and 81-86 of this instant application. Further, the process of generating gene clusters or gene expression profiles is a type of recursive partitioning, as in claim 92 of this instant application.



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51. KEGG can be accessed at the following address: <http://www.genome.ad.jp/kegg/>. The KEGG mirror server package may be installed. The package, which also includes a minimal set of DBGET/LinkDB, can be obtained from the KEGG anonymous FTP site: <ftp://kegg.genome.ad.jp/>. The mirror package runs on a Solaris or IRIX machine. The individual databases PATHWAY, GENES, and LIGAND can also be obtained from this FTP site. The CD version of KEGG was once distributed and a copy still exists at the FTP site. Some of the search tools are also available at the KEGG mail server (Page 34, Column 2, Lines 9-26). The disclosure by Ogata et al. above anticipates the limitations of claims 1, 46, 57, 59 and 133.

### **CONCLUSION**

52. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

53. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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54. This application contains claims 4-9, 11-13, 24-26, 29-32, 58, 65, 66, 69, and 111-119 drawn to an invention nonelected with traverse in the previous Office Action, mailed March 10, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.


55. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

56. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

57. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

58. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly  
11/28/03

  
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